

# Tetanus

**T**ETANUS IS AN ACUTE, OFTEN FATAL, DISEASE CAUSED by an exotoxin produced by *Clostridium tetani*. It is characterized by generalized rigidity and convulsive spasms of skeletal muscles. The muscle stiffness usually involves the jaw (lockjaw) and neck and then becomes generalized.

Although records from antiquity (5th century B.C.) contain clinical descriptions of tetanus, it was Carle and Rattone who first produced tetanus in animals by injecting them with pus from a fatal human tetanus case in 1884. During the same year, Nicolaier produced tetanus in animals by injecting them with samples of soil. In 1889, Kitasato isolated the organism from a human victim, showed that it produced disease when injected into animals, and reported that the toxin could be neutralized by specific antibodies. In 1897, Nocard demonstrated the protective effect of passively transferred antitoxin, and passive immunization in humans was used during World War I. Tetanus toxoid was described by Descombey in 1924, and the effectiveness of active immunization was demonstrated in World War II.

## *Clostridium tetani*

*C. tetani* is a slender, gram-positive, anaerobic rod that may develop a terminal spore, giving it a drumstick appearance. The organism is sensitive to heat and cannot survive in the presence of oxygen. The spores, in contrast, are very resistant to heat and the usual antiseptics. They can survive autoclaving at 121° C for 10-15 minutes. The spores are also relatively resistant to phenol and other chemical agents.

The bacilli are widely distributed in soil and in the intestine and feces of horses, sheep, cattle, dogs, cats, rats, guinea pigs, and chickens. Manure-treated soil may contain large numbers of spores. In agricultural areas, a significant number of human adults may harbor the organism. The spores can also be found on skin surfaces and in contaminated heroin.

### Tetanus

- Toxin mediated
- First described by Hippocrates
- Etiology discovered in 1884 by Carle and Rattone
- Passive immunity used for treatment and prophylaxis during World War I
- Tetanus toxoid first widely used during World War II

### *Clostridium tetani*

- Anaerobic gram-positive, spore-forming bacteria
- Spores found in soil, dust, animal feces; may persist for months to years
- Multiple toxins produced with growth of bacteria
- Tetanospasmin estimated human lethal dose = 150 ng

### Tetanus - Pathogenesis

- Anaerobic conditions allow germination of spores and production of toxins.
- Toxin binds in central nervous system
- Interferes with neurotransmitter release to block inhibitor impulses.
- Leads to unopposed muscle contraction and spasm.

### Tetanus - Clinical Features

- Incubation period 8 days (range, 3-21 days)
- Three clinical forms: Local (uncommon), cephalic (rare), generalized (most common)
- Generalized tetanus: descending symptoms of trismus (lockjaw), difficulty swallowing, muscle rigidity, spasms
- Spasms continue for 3-4 weeks; complete recovery may take months

## Pathogenesis

*C. tetani* usually enters the body through a wound. In the presence of anaerobic (low oxygen) conditions, the spores germinate. Toxins, including tetanospasmin, are produced, and disseminated via blood and lymphatics. Toxins act at several sites within the central nervous system, including peripheral motor end plates, spinal cord, brain, and sympathetic nervous system. The typical clinical manifestations of tetanus are caused when tetanus toxin interferes with release of neurotransmitters, blocking inhibitor impulses. This leads to unopposed muscle contraction and spasm. Seizures may occur, and the autonomic nervous system may also be affected.

## Clinical Features

The **incubation period** varies from 3 to 21 days, usually about 8 days. In general the further the injury site is from the central nervous system, the longer the incubation period. The shorter the incubation period, the higher the chance of death. In neonatal tetanus, symptoms usually appear from 4 to 14 days after birth, averaging about 7 days.

On the basis of clinical findings, three different forms of tetanus have been described.

**Local tetanus** is an uncommon form of the disease, in which patients have persistent contraction of muscles in the same anatomic area as the injury preceding the tetanus. These contractions may persist for many weeks before gradually subsiding. Local tetanus may precede the onset of generalized tetanus, but is generally milder. Only about 1% of cases are fatal.

**Cephalic tetanus** is a rare form of the disease, occasionally occurring with otitis media (ear infections) in which *C. tetani* is present in the flora of the middle ear, or following injuries to the head. There is involvement of the cranial nerves, especially in the facial area.

The most common type (about 80%) of reported tetanus is **generalized tetanus**. The disease usually presents with a descending pattern. The first sign is trismus or lockjaw, followed by stiffness of the neck, difficulty in swallowing, and rigidity of abdominal muscles. Other symptoms include a temperature rise of 2°-4°C above normal, sweating, elevated blood pressure, and episodic rapid heart rate. Spasms may occur frequently and last for several minutes. Spasms continue for 3-4 weeks. Complete recovery may take months.

**Neonatal tetanus** is a form of generalized tetanus that occurs in newborn infants. Neonatal tetanus occurs in infants born without protective passive immunity, because the mother is not immune. It usually occurs through infection of the unhealed umbilical stump, particularly when the stump is cut with an unsterile instrument. Neonatal tetanus is common in some developing countries (estimated >270,000 deaths worldwide per year), but very rare in the United States.

## Complications

**Laryngospasm** (spasm of the vocal cords) and/or spasm of the muscles of respiration leads to interference with breathing. **Fractures of the spine or long bones** may result from sustained contractions and convulsions.

**Hyperactivity of the autonomic nervous system** may lead to hypertension and/or an abnormal heart rhythm.

**Nosocomial infections** are common because of prolonged hospitalization. Secondary infections, which may include sepsis from indwelling catheters, hospital-acquired pneumonias, and decubitus ulcers. **Pulmonary embolism** is particularly a problem in drug users and elderly patients. **Aspiration pneumonia** is a common late complication of tetanus, found in 50%-70% of autopsied cases.

**Death.** Approximately 30% of reported cases are fatal. In the United States, most deaths occur in persons >50 years of age. In about 20% of tetanus deaths, no obvious pathology is identified and death is attributed to the direct effects of tetanus toxin. The course usually lasts several weeks, with gradual decline over time.

Due to the extreme potency of the toxin, tetanus disease does not confer immunity. Patients who survive the disease should be given a complete series of vaccine.

## Laboratory Diagnosis

There are no laboratory findings characteristic of tetanus. The diagnosis is entirely clinical and does not depend upon bacteriologic confirmation. *C. tetani* is recovered from the wound in only 30% of cases, and not infrequently it is isolated from patients who do not have tetanus. Laboratory identification of the organism depends most importantly on the demonstration of toxin production in mice.

### Neonatal Tetanus

- Generalized tetanus in newborn infant
- Infant born without protective passive immunity
- High fatality rate without therapy
- Estimated 270,000 deaths worldwide in 1998

### Tetanus Complications

- |                |   |
|----------------|---|
| • Laryngospasm | Spasms of vocal cords and respiratory muscles                             |
| • Fractures    | Spine and long bones due to muscle spasms and seizures                    |
| • Other        | Hypertension, coma, nosocomial infections, pulmonary embolism, aspiration |
| • Death        | 30%, higher at extremes of age  |

## Medical Management

All wounds should be cleaned necrotic tissue and foreign material should be removed. If tetanic spasms are occurring, supportive therapy, primarily maintenance of an adequate airway, are critical.

Tetanus immune globulin (TIG) is recommended for persons with tetanus. TIG can only help remove unbound tetanus toxin. It cannot effect toxin bound to nerve endings. A single intramuscular dose of 3000 to 5000 units is generally recommended for children and adults, with part of the dose infiltrated around the wound if it can be identified. Intravenous immune globulin (IVIG) contains tetanus antitoxin and may be used if TIG is not available.

Tetanus disease does not result in tetanus immunity. Active immunization with tetanus toxoid should begin or continue as soon as the person's condition has stabilized.

## Wound Management

Antibiotic prophylaxis against tetanus is neither practical nor useful in managing wounds; proper immunization plays the more important role. The need for active immunization, with or without passive immunization, depends on the condition of the wound and the patient's immunization history (see table). Rarely have cases of tetanus occurred in persons with a documented primary series of tetanus toxoid.

Persons with wounds that are neither clean nor minor, and who have had 0-2 prior doses or have an uncertain history of prior doses, need tetanus immune globulin (TIG) as well as Td toxoids. This is because early doses of toxoid do not induce immunity, but only prime the immune system. The TIG provides temporary immunity by directly providing antitoxin. This ensures that protective levels of antitoxin are achieved even if an immune response has not yet occurred.

## Epidemiology

### Occurrence

Occurrence is worldwide, but is most frequently encountered in densely populated regions in hot, damp climates with soil rich in organic matter.

### Reservoir

Organisms are found primarily in the soil and intestinal tracts of animals and humans.

**Tetanus  
Wound Management**

Vaccination History	Clean, minor wounds		All other wounds	
	Td	TIG	Td	TIG
Unknown or <3 doses	Yes	No	Yes	Yes
3+ doses	No*	No	No**	No

\* Yes, if >10 years since last dose

\*\* Yes, if >5 years since last dose

**Tetanus  
Epidemiology**

• Reservoir	Soil and intestine of animals and humans
• Transmission	Contaminated wounds Tissue injury
• Temporal pattern	Peak in summer or wet season
• Communicability	Not contagious

### Mode of transmission

Transmission is primarily by contaminated wounds (apparent and inapparent). The wound may be major or minor. In recent years, however, a higher proportion of cases had minor wounds, probably because severe wounds are more likely to be properly managed. Tetanus may follow elective surgery, burns, deep puncture wounds, crush wounds, otitis media (ear infections), dental infection, animal bites, abortion, and pregnancy.

### Communicability

Tetanus is not contagious from person to person. It is the only vaccine-preventable disease that is infectious, but not contagious.

### Secular Trends in the United States

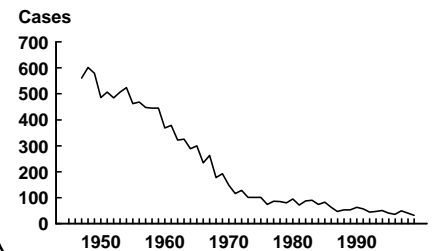
A marked decrease in mortality occurred from the early 1900s to the late 1940s. In the late 1940s, tetanus toxoid was introduced into routine childhood immunization and tetanus became nationally notifiable. At that time, there were 500-600 cases reported per year (approximately 0.4 cases per 100,000 population).

After the 1940s, reported tetanus incidence rates fell steadily. Since the mid-1970s, 50-100 cases have been reported annually (~ 0.05 cases per 100,000). The death-to-case ratio has been relatively constant at approximately 30%. A provisional all-time low of 33 cases (0.02 cases per 100,000) were reported in 1999.

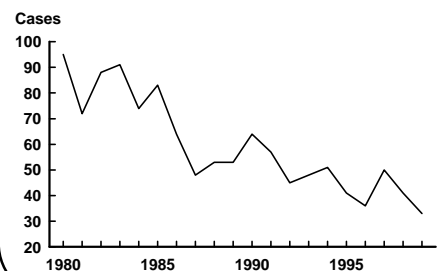
From 1982 through 1998, 63% of reported cases were among persons 50 years of age or older, and 52% were among persons 60 and older. The age distribution of reported cases has shifted to a younger age group in the last few years. From 1995 to 1997, people 20 to 59 accounted for 60% of all cases, with people 60 and older accounting for only 35 percent. The reason for this recent change in age distribution is both an increase in cases in 20 to 59 year olds, and a decrease in cases in older people. The increase in cases in 20 to 59 year olds is related in part to an increased number of cases among injection drug users in California.

Almost all reported cases of tetanus are in persons who have either never been vaccinated, or who completed a primary series, but have not had a booster in the preceding 10 years.

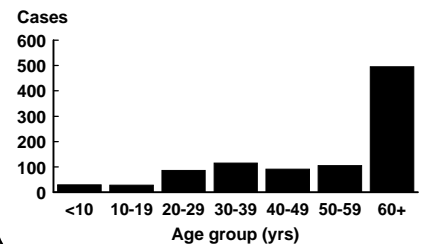
**Tetanus - United States, 1947-1999**



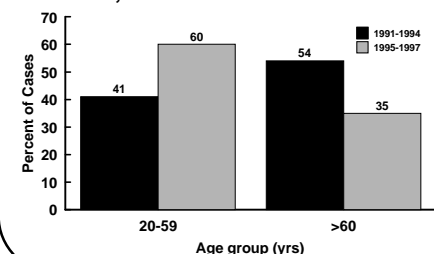
**Tetanus - United States, 1980-1999**



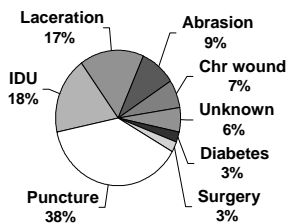
**Tetanus - United States, 1982-1998  
Age Distribution of Reported Cases**



**Age Distribution of Reported Tetanus Cases, 1991-1994 and 1995-1997**



### Tetanus - 1995-1997 Injuries and Conditions



Data available for 120 of 124 reported cases

Heroin users, particularly persons who inject themselves subcutaneously with quinine, appear to be at high risk for tetanus. Quinine is used to dilute heroin and may actually be predisposed to growth of *C. tetani*.

Neonatal tetanus is rare in the United States, with only 2 cases reported since 1989. Neither of the infants' mothers had ever received tetanus toxoid.

During 1995-1997, acute injuries such as punctures, lacerations and abrasions accounted for 64% of reported cases of tetanus. Thirteen of those with acute injuries reported stepping on a nail. Other acute injuries included self-performed body piercing and tattooing, animal bites and splinters. Twenty-two (18%) of cases reported injection drug use (IDU). About half of the IDU-related cases reported a wound, such as an abscess at the site of injection. Three cases were reported after surgical procedures (hemorrhoid banding, spine implant, knee surgery). Eight cases had various chronic wounds. Three had diabetes mellitus without a known injury or wound. The type of injury or condition was unknown for 8 reported cases.

## Tetanus Toxoid

### Characteristics

Tetanus toxoid has proved to be safe and useful since Descombey first reported its production in 1924. Tetanus toxoid immunizations were used extensively in the armed services during World War II. Tetanus cases among this population dropped from 70 in World War I (13.4/100,000 wounds and injuries) to 12 in World War II (0.44/100,000). Of the 12 cases, half had received no prior toxoid.

Tetanus toxoid consists of a formaldehyde-treated toxin. The toxoid is standardized for potency in animal tests according to Food and Drug Administration (FDA) regulations. Occasionally, potency is mistakenly equated with Lf units, which are a measure of the quantity of toxoid, not its potency in inducing protection.

There are two types of toxoid available — adsorbed (aluminum salt precipitated) toxoid and fluid toxoid. Although the rates of seroconversions are about equal, the adsorbed toxoid is preferred because the antitoxin response reaches higher titers and is longer lasting than following the fluid toxoid.

Tetanus toxoid is available as a single antigen preparation, combined with diphtheria as pediatric DT or adult Td, and with both diphtheria toxoid and acellular pertussis vaccine as DTaP. Combination diphtheria and tetanus toxoids and

### DTaP, DT, and Td

	Diphtheria	Tetanus
DTaP, DT	7-8 Lf units	5-12.5 Lf units

Td (adult)	2 Lf units	5 Lf units
Pertussis vaccine and pediatric DT used through age 6 years. Adult Td used for persons 7 years and older.		

whole cell pertussis vaccine (DTP) is available but is no longer recommended. Pediatric formulations (DT and DTaP) contain a similar amount of tetanus toxoid as adult Td, but contain 3-4 times as much diphtheria toxoid. Children younger than 7 years of age should receive either DTaP or pediatric DT. Persons 7 years of age or older should receive the adult formulation (adult Td), even if they have not completed a series of DTaP or pediatric DT. There is virtually no reason to use single antigen tetanus toxoid. Tetanus toxoid should be given in combination with diphtheria toxoid, since periodic boosting is needed for both antigens.

### *Immunogenicity and vaccine efficacy*

After a primary series of three properly spaced doses of tetanus toxoid in persons >7 years of age and four doses in children <7 years of age, essentially all recipients achieve antitoxin levels considerably greater than the minimal protective level of 0.01 IU/ml.

Efficacy of the toxoid has never been studied in a vaccine trial. It can be inferred from protective antitoxin levels that a complete tetanus toxoid series has a clinical efficacy of virtually 100%; cases of tetanus occurring in fully immunized persons whose last dose was within the last 10 years are extremely rare.

Following a properly administered primary series, virtually all persons develop a protective level of antitoxin. Antitoxin levels fall over time. While some persons may be protected for life, most persons have antitoxin levels that approach the minimal protective level by 10 years after the last dose. As a result, routine boosters are recommended every 10 years.

In a small percentage of individuals, antitoxin levels fall below the minimal protective level before 10 years have elapsed. To ensure adequate protective antitoxin levels in individuals who sustain a wound that is other than clean and minor, a booster is recommended for these people if more than 5 years have elapsed since their last dose. (See **Wound Management** for details on persons who previously received fewer than three doses.)

### **Vaccination Schedule and Use**

Primary tetanus immunization, usually as combined with diphtheria toxoid and acellular pertussis vaccine (DTaP), is recommended for all persons at least 6 weeks old, but less than 7 years of age, for whom the vaccine is not contraindicated. The recommended routine primary vaccina-

#### **Tetanus Toxoid**

- Formalin-inactivated tetanus toxin
- Schedule Three or four doses + booster  
Booster every 10 years
- Efficacy Approximately 100%
- Duration Approximately 10 years
- Should be administered with diphtheria toxoid as DTaP, DT, or Td

#### **Routine DTaP Primary Vaccination Schedule**

Dose	Age	Interval
Primary 1	2 months	---
Primary 2	4 months	4 wks
Primary 3	6 months	4 wks
Primary 4	15-18 months	6 mos

### Routine DTaP Schedule Children <7 years of age

#### Booster Doses

- 4-6 years, before entering school
- 11-12 years of age if >5 years since last dose (Td)
- Every 10 years thereafter (Td)

### Routine Td Schedule Persons >7 years of age

Dose	Interval
Primary 1	---
Primary 2	4 wks
Primary 3	6-12 mos

Booster dose every 10 years

### Diphtheria and Tetanus Toxoid Adverse Events

- Local reactions (erythema, induration)
- Nodule at injection site
- Hypersensitivity reactions (Arthus-type)
- Fever and systemic symptoms uncommon
- Severe systemic reactions rare

tion schedule is four doses at 2, 4, 6, and 15-18 months of age. If a child has a valid contraindication to pertussis vaccine, pediatric DT should be used to complete the vaccination series.

A minimum of 4 weeks (typically 6-8 weeks) should separate the first and second, and second and third doses of tetanus toxoid. The fourth dose of the primary series should be given no less than 6 months after the third dose. If the fourth dose of DTaP, DTP, or DT is administered before the fourth birthday, a booster dose is recommended at 4-6 years of age.

Because of waning antitoxin titers, most individuals have antitoxin levels below optimal levels 10 years after the last dose of DTaP, DTP, DT, or Td. As a result, additional booster doses of tetanus and diphtheria toxoids (as Td) are required every 10 years to maintain protective antitoxin titers. The first booster dose may be given at 11-12 years of age, if at least 5 years have elapsed since the last dose of DTaP, DTP, or DT. If a dose is given sooner as part of wound management, the next booster is not needed for 10 years thereafter. More frequent boosters are not indicated and have been reported to result in an increased incidence and severity of local adverse reactions.

Adult Td, is the vaccine of choice for routine vaccination of all persons 7 years old and older. Three doses constitute a primary series of Td. The first two doses are separated by a minimum of 4 weeks, with the third dose given 6-12 months after the second.

Tetanus disease does not confer immunity because of the very small amount of toxin required to produce illness. Persons recovering from tetanus should begin or complete active immunization with tetanus toxoid (Td) during convalescence.

## Adverse Reactions Following Vaccination

**Local adverse events** (*e.g.*, erythema, induration, pain at the injection site) are common, but are usually self-limited and require no therapy. A nodule may be palpable at the injection site of adsorbed products for several weeks. Abscess at the site of injection has been reported. Fever and other systemic symptoms are uncommon.

**Exaggerated local (Arthus-like) reactions** are occasionally reported following receipt of a tetanus-containing vaccine. These unusual reactions present as extensive painful swelling, often from shoulder to elbow. They generally begin from 2 to 8 hours after injections, and are reported most often in adults, particularly those

who have received frequent doses of tetanus toxoid. Persons experiencing these severe reactions usually have very high serum tetanus antitoxin levels; they should not be given further routine or emergency booster doses of Td more frequently than every 10 years. Less severe hypersensitivity local reactions may occur in persons who have multiple prior boosters.

**Severe systemic reactions** such as generalized urticaria (hives), anaphylaxis, or neurologic complications have been reported after receipt of tetanus toxoid. A few cases of peripheral neuropathy and Guillain-Barré Syndrome (GBS) have been reported following tetanus toxoid administration. Following a recent review, the Institute of Medicine concluded that the available evidence favors a causal relationship between tetanus toxoid and both brachial neuritis and GBS, although these reactions are very rare.

## Contraindications and Precautions to Vaccination

A **severe allergic reaction** (acute respiratory distress or collapse) following a previous dose of tetanus toxoid is a contraindication to receipt of tetanus toxoid. If a generalized reaction is suspected to represent allergy, it may be useful to refer an individual for appropriate skin testing before discontinuing tetanus toxoid immunization.

A **moderate or severe acute illness** is reason to defer routine vaccination, but a minor illness is not.

If a contraindication to using tetanus toxoid-containing preparations exists, passive immunization with tetanus immune globulin (TIG) against tetanus should be considered whenever an injury other than a clean minor wound is sustained.

## Vaccine Storage and Handling

DTP vaccine, DT (pediatric), Td, DTP/Hib, DTaP, and tetanus toxoid should be stored continuously at 2°-8°C (35°-46°F). The vaccine may be out of refrigeration for up to 4 days, but should be refrigerated immediately when received. Freezing reduces the potency of the tetanus component.

### Diphtheria and Tetanus Toxoids Contraindications and Precautions

- Severe allergic reaction to vaccine component or following prior dose
- Moderate or severe acute illness

### Tetanus Summary

- Toxin mediated and noncontagious
- 40-60 reported cases per year
- Most cases in older persons, high fatality rate
- Need for adult immunization

## Selected References

CDC. Diphtheria, tetanus, and pertussis: Recommendations for vaccine use and other preventive measures: Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1991;40(RR-10):1-28.

CDC. Tetanus surveillance--United States, 1995-1997. *MMWR* 1998;47 (SS-2):1-13.

Evans AS and Brachman PS, eds. *Bacterial Infections of Humans. Epidemiology and Control*. 3rd edition. New York, NY: Plenum Medical Book Company, 1998.

Kumar S, Malecki JM. A case of neonatal tetanus. *South Med J* 1991;84: 396-8.

Peter G, ed. *1997 Red Book: Report of the Committee on Infectious Diseases*. 24th ed. Elk Grove Village, IL: American Academy of Pediatrics, 1997.

Plotkin SA, Orenstein, WA, eds. *Vaccines*. 3rd edition. Philadelphia: W.B. Saunders Company, 1999.

Orenstein WA, Hadler S, Wharton M. Trends in vaccine-preventable diseases. *Semin Pediatr Infect Dis* 1997;8:23-33.

Sutter RW, Cochi SL, Sirotkin B, et al. Assessment of vital statistics and surveillance data for monitoring tetanus mortality, United States, 1979-1984. *Am J Epidemiol* 1990;131: 132-42.

World Health Organization. The "high-risk" approach: the WHO-recommended strategy to accelerate elimination of neonatal tetanus. *Wkly Epidemiol Rec* 1996;71:33-6.